

DETAILED ACTION
RESPONSE TO ARGUMENTS

35 USC § 103

The rejection of claims 1-8 under 35 U.S.C. 103(a) as being unpatentable over Ramsby et al. (Electrophoresis. Feb 1994; 15(2): 265-277) and further in view of Robaye et al. (Electrophoresis. 1994; 15: 503-510) and further in view of Squier et al. (Journal of Cellular Physiology, May 1994; 159(2): 229-237) and further in view of Lowe et al. (Nature. 29 April 1993; 362: 847-849) further in view of Lane et al (*British Medical Bulletin*. 1994; 50(3):582-599) is withdrawn in response to the applicant's Appeal Brief arguments. The applicant's arguments have been fully considered and are persuasive. Therefore, the examiner hereby withdraws the rejection of claims 1-8 under 35 USC 103(a) as being unpatentable over Ramsby et al. in view of Robaye et al. and further in view of Squier et al. and further in view of Lowe et al. further in view of Lane et al.

EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with David Kulik on 7/19/2010.

Art Unit: 1633

The claims have been amended as follows:

1. (Amended) A method for detecting an inhibitor of p53 protein degradation comprising providing a cell extract containing one or more p53 protein and one or more proteases, administering a peptide or protein inhibitor of calpain protease activity of to the cell extract, and measuring p53 protein and p53 protein fragments, wherein the inhibitor administered is a calpastatin.

Claims 2 and 6 are cancelled.

3. (Amended) The method of claim [[2]] 1, wherein the calpastatin is encoded by one of SEQ ID NO: 1-3.

Reasons for Allowance

The following is an examiner's statement of reasons for allowance:

The prosecution history provides evidence for allowability.

During an examiner-initiated interview, the examiner told the applicant's representative that 35 UC 102 rejections of claims 1, 4, 8 could be made over Huibregtse which would require that the examiner reopen prosecution after the applicant had filed an Appeal Brief.

Prior to Examiner's Amendment, claim 1 was directed to a method for detecting an inhibitor of p53 protein degradation comprising providing a cell extract containing one or more p53 proteins and one or more proteases, administering a peptide or protein inhibitor of calpain protease activity to the cell extract, and measuring p53 protein and p53 protein fragments.

Huibregtse et al. (Molecular and Cellular Biology. Aug. 1993; 13(8): 4918-4927) teach preparing a cell extract of Sf9 insect cells using a lysis buffer comprising leupeptin (page 4920, col.1, *Ubiquitination assays* section). Leupeptin is a calpain protease inhibitor. Huibregtse et al. teach measuring p53 protein by SDS-PAGE (Fig. 5B). Accordingly, Huibregtse et al. anticipate claims 1 & 8 under 35 USC 102(a).

Huibregtse et al. (EMBO Journal. 1991; 10(13): 4129-4135) teach preparing a cell extract of HeLa, C-33A, and Saos-2 cells using a lysis buffer comprising leupeptin (page 4134, *Preparation of Cell Extracts* section). Leupeptin is a calpain protease inhibitor. Huibregtse et al. teach measuring p53 protein by SDS-PAGE (Fig. 1). Accordingly, Huibregtse et al. anticipated claims 1, 4 and 8 under 35 USC 102(b).

The examiner observed that dependent claims contained elements which were non-obvious over the cited art and if incorporated into the independent claim would be allowable. The examiner proposed an Examiner's amendment to move the limitations of claim 2 into independent claim 1. After consulting with the applicant, the applicant's representative granted permission for this Examiner's amendment on Monday July 19, 2010.

As the examiner understands the novel feature of the applicant's invention, the

Art Unit: 1633

applicant is establishing a nexus between calpastatin's specific inhibition of calpain and calpain's degradation of p53. This nexus was not obvious, based on the prior art available at the time of filing. The applicant's have an extremely early effective filing date in this field, 31 May 1994, from the foreign application FRANCE FR94/06583. The examiner was unable to provide sound scientific reasoning to detect inhibitors of p53 degradation, based upon inclusion of calpastatin in a protease inhibitor cocktail used to treat cell extracts. While measuring p53 in cell extracts treated with protease inhibitor cocktail containing leupeptin and aprotinin is well know, as taught by Huibregtse et al. and calpastatin had been identified as a calpain-specific protease inhibitor, as was known at the time of filing, the link between these facts had not been made prior to the claimed invention. Accordingly, the examiner finds an Examiner's Amendment to move the limitations of claim 2 into independent claim 1 would be non-obvious.

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Conclusion

Claims 1, 3-5 and 7-8 are allowed.

Examiner Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Scott Long** whose telephone number is **571-272-9048**.

The examiner can normally be reached on Monday - Friday, 9am - 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Joseph Woitach** can be reached on **571-272-0739**. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/SCOTT LONG/
Primary Examiner, Art Unit 1633